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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,317	12/03/2003	Akito Ichida	Furuya Case 1410	6210
1095	7590	08/24/2004	EXAMINER OH, TAYLOR V	
NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 430/2 EAST HANOVER, NJ 07936-1080			ART UNIT 1625	PAPER NUMBER
DATE MAILED: 08/24/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/727,317

Applicant(s)

ICHIDA, AKITO

Examiner

Taylor Victor Oh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 7/04 & 12/03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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The Status of Claims:

Claims 1-5 are pending.

Claims 1-5 have been rejected.

DETAILED ACTION

Priority

1. It is noted that applicants have satisfied the requirement of 35 USC 119 by filing priority document ,JP 2003-018299, January, 28, 2003.

Drawings

2. None.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 5, the phrase “ 3-chloro-5-nitrotoluene obtained by any process ” is recited. The expression of the term “ any process” is improper because the

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process of obtaining 3-chloro-5-nitrotoluene is defined by claim 1. Therefore, an appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Grella et al (J. Med. Chem. P. 4726-4737, 2000).

Grella et al discloses the preparation of 3-chloro-5-nitrotoluene in the following procedures (see page 4733, right column, lines 19-44):

2-Chloro-4-methyl-6-nitroaniline (23). A mixture of 4-methyl-2-nitroaniline (50.0 g, 329 mmol) and *N*-chlorosuccinimide (70.3 g, 526 mmol) was refluxed in acetonitrile (200 mL) overnight. Removal of acetonitrile under reduced pressure, afforded a dark red crude oil mixture. The mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 7:1–6:1) to obtain a dark orange solid, 17.6 g, 29%. Mp: 55–58 °C. ¹H NMR (CDCl₃): δ 2.28 (s, 3H), 6.41 (s, 2H), 7.38 (s, 1H), 7.90 (s, 1H).

3-Chloro-5-nitrotoluene (24). A solution of 23 (17.5 g, 94.4 mmol) in ethanol (100 mL) was allowed to cool to 0 °C and concentrated sulfuric acid was added (20 mL). Sodium nitrite (40 wt % solution in water, 13.0 g, 189 mmol) was added dropwise to the solution, and the reaction mixture was allowed to warm to room temperature and stirred for 30 min. Then the mixture was refluxed until the evolution of nitrogen gas ceased. The reaction mixture was concentrated under reduced pressure and then diluted with water (100 mL) and extracted with ethyl acetate (4 × 75 mL). The combined organic fractions were washed with brine, dried over anhydrous MgSO₄, and the solvent was removed under reduced pressure to afford a dark red oil. The product was purified by flash chromatography (eluent: hexane/ethyl acetate 7:1) to give an orange solid, 11.2 g, 69%. Mp: 55–57 °C. ¹H NMR (CDCl₃): δ 2.46 (s, 3H), 7.50 (s, 1H), 7.94 (s, 1H), 8.03 (s, 1H).

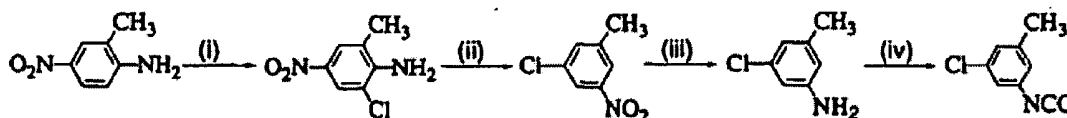
This is identical with the claims.

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Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Chankvetadze et al (J. of Chromatography A, 787, (1997) p. 67-77) .

Chankvetadze et al discloses the synthesis of 3-chloro-5-methylphenylisocyanate in below:

(b) Synthesis of 3-chloro-5-methylphenyl isocyanate



Reagent and conditions: (i) KClO_4 , quant.; (ii) $\text{NaNO}_2\text{-H}_2\text{SO}_4$, in EtOH, quant.; (iii) SnCl_2 in 95% EtOH, HCl, 73%; (iv) HCl, triphosgene in toluene, 43%.

This is identical with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grella et al (J. Med. Chem. P. 4726-4737, 2000) in view of Metzger (U.S. 3,972,910).

Grella et al discloses the preparation of 3-chloro-5-nitrotoluene in the following procedures (see page 4733, right column, lines 19-44):

2-Chloro-4-methyl-6-nitroaniline (23). A mixture of 4-methyl-2-nitroaniline (50.0 g, 329 mmol) and *N*-chlorosuccinimide (70.3 g, 526 mmol) was refluxed in acetonitrile (200 mL) overnight. Removal of acetonitrile under reduced pressure, afforded a dark red crude oil mixture. The mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 7:1→6:1) to obtain a dark orange solid, 17.6 g, 29%. Mp: 55–58 °C. ¹H NMR (CDCl₃): δ 2.28 (s, 3H), 6.41 (s, 2H), 7.38 (s, 1H), 7.90 (s, 1H).

3-Chloro-5-nitrotoluene (24). A solution of 23 (17.5 g, 94.4 mmol) in ethanol (100 mL) was allowed to cool to 0 °C and concentrated sulfuric acid was added (20 mL). Sodium nitrite (40 wt % solution in water, 13.0 g, 189 mmol) was added dropwise to the solution, and the reaction mixture was allowed to warm to room temperature and stirred for 30 min. Then the mixture was refluxed until the evolution of nitrogen gas ceased. The reaction mixture was concentrated under reduced pressure and then diluted with water (100 mL) and extracted with ethyl acetate (4 × 75 mL). The combined organic fractions were washed with brine, dried over anhydrous MgSO₄, and the solvent was removed under reduced pressure to afford a dark red oil. The product was purified by flash chromatography (eluent: hexane/ethyl acetate 7:1) to give an orange solid, 11.2 g, 69%. Mp: 55–57 °C. ¹H NMR (CDCl₃): δ 2.46 (s, 3H), 7.50 (s, 1H), 7.94 (s, 1H), 8.03 (s, 1H).

However, the instant invention differs from the prior art in that the claimed chlorinating agent is *t*-butylhypochlorite; and the reaction mixture is maintained at a temperature of 40 to 50 °C during the deamination process.

Metzger teaches that the toluene ring can be chlorinated; for example, 2,4- and /or 2,6-toluene diamine is reacted with *N*-chlorosuccinimide, *t*-butylhypochlorite, or the like (see col. 2, lines 43-51).

Concerning the variation of the reaction temperature from 40 to 50 °C

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during the deamination process, Grella et al is silent; however, Grella et al has indicated that after adding sodium nitrite to the reaction mixture, the deamination is conducted between zero and room temperature and then the mixture is refluxed. With the Grella's et al guidance, it is possible that, during the deamination process, the reaction mixture has been allowed to have the temperature variations of 40 to 50 °C. Furthermore, The limitation of a process with respect to ranges of pH, time and temperature does not impart patentability to a process when such values are those which would be determined by one of ordinary skill in the art in achieving optimum operation of the process.

Temperature is well understood by those of ordinary skill in the art to be a result-effective variable, especially when attempting to control selectivity in a chemical process.

Grella et al expressly teaches the preparation of 3-chloro-5-nitrotoluene by reacting 2-methyl-4-nitroaniline with the N-chlorosuccinimide chlorinating agent. Similarly, Metzger also teaches that the chlorination of the aminotoluene ring can be achieved either by N-chlorosuccinimide or t-butylhypochlorite (see col. 2, lines 43-51). From this, there is a teaching of equivalence between N-chlorosuccinimide and t-butylhypochlorite. Furthermore, both prior art have been dealt with the chlorination of the aromatic compound with the substituents of methyl and amino groups. With the guidance of the Metzger teaching, therefore, it would have been obvious to the skilled artisan in the art to be motivated to employ Metzger's t-butylhypochlorite as an alternative to the N-chlorosuccinimide

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chlorinating agent in the Grella et al process because the skilled artisan in the art would expect such a modification to be effective and successful as shown in the Metzger.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached from 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

R. Desai
8/20/04.
for Cecilia Tsang.